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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,903	MORRIS ET AL.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,38,40-45,48,52,54,55,58 and 79-98* is/are pending in the application.

4a) Of the above claim(s) *32,38,40-45,48,54,55,58 and 95-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52 and 79-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group VI (claims 52 and 79-94, specie of kidney cancer) in the reply filed on November 25, 2009 is acknowledged. The traversal is on the ground(s) that:

"Applicants submit that, while the claims of Group VI are patentably distinct from the claims of Groups I-V, VII and VIII, a thorough search of the elected claims of Group VI will include art relevant to the claims of the remaining Groups. In particular, a thorough search of SEQ ID NO: 41 recited in Group VI, directed to a method for diagnosing kidney, colon, prostate, breast or stomach cancer comprising employing SEQ ID NO:41, will encompass the methods of Groups I-V, VII and VIII because all Groups of claims are directed to a diagnostic or detection method using SEQ ID NO: 41.

For example, Group I, claims 32 and 38, is directed to a method of screening for anticancer activity of a drug candidate using SEQ ID NO: 41. Group II, claims 40, 41 and 79-94, is directed to a method for detecting cancer using SEQ ID NO: 41. Group III, claim 42, is directed to a method for detecting cancer using SEQ ID NO: 41. Group IV, claim 43, is directed to a method for detecting cancer using the polypeptide encoded by SEQ ID NO: 41. Group V, claims 44, 45 and 48, is directed to a method for screening for a bioactive agent using SEQ ID NO:41. Group VII, claims 54, 55 and 58, is directed to a method for treating cancer by administering an inhibitor of SEQ ID NO: 41. While Group VIII, claims 95-98, is directed to a method of diagnosing kidney, colon, prostate, breast or stomach cancer using SEQ ID NO: 41 under specified hybridization conditions. Accordingly, the joint examination of claims 32, 38,

40-45, 48, 52, 54, 55, 58 and 79-88 will not result in a serious burden on the Examiner and rejoinder of all Groups is respectfully is requested."

This is not found persuasive because search for methods of these different groups involves more than just a sequence search. Each of these methods uses SEQ ID NO: 41 in a different way, either as a nucleic acid or polypeptide encoded by it. As Applicants realize, search for SEQ ID NO: 41 is not going to reveal art pertaining to an antibody binding to a polypeptide encoded by SEQ ID NO: 41. Finally, all of these different methods present different issues under 35 U.S.C. 112, first paragraph.

Applicants further argue that examiner should consider all of the claimed cancers, Again, because sequence search will provide art related to all claimed cancers. It does not, and, again, the different species have different issues under 35 U.S.C. 112, first paragraph.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 32, 38, 40-45, 48, 54, 55, 58 and 95-98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 25, 2009.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

4. Claims 52 and 79-94 will be examined with respect to detection of kidney cancer.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on August 21, 2007 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

The disclosure is objected to because of the following informalities:

A) The first paragraph contains a list of applications which are "related" to the instant application. It is not clear whether any of these applications is meant to be claimed as a priority application, and if so, what is their relationship to the instant application. Further, two of the applications are listed by their docket numbers, rather than by their application number.

B) On page 32, paragraph [0099], the international applications are listed by their PCT numbers, rather than by their WO publication numbers.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 52 and 79-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species

situations that "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID NO: 41. Specifically, Applicants claim a method of diagnosing cancer by detecting a level of expression of a nucleic acid with 95% or 98% sequence identity to SEQ ID NO: 41 or complements thereof. First, Applicants showed that SEQ ID NO: 41 is overexpressed in 1 out of 12 renal cell carcinomas, which is not an indication that SEQ ID NO: 41 has diagnostic potential in kidney cancer. Then, Applicants did not show that any other nucleic acids related to SEQ ID NO: 41, such as sequences having 95 or 98% identity to SEQ ID NO: 41 were upregulated in any cancers. The genus of sequences with 95% sequence identity to SEQ ID NO: 41 (4099 bp) has $4^{205} = 9.6 \times 10^{123}$ members, and the genus of sequences 98% identical to SEQ ID NO: 41 has $4^{82} = 1.2 \times 10^{49}$ members.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516,

> 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the sequences 95% or 98% identical to SEQ ID NO: 41 lack any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for one specific sequence, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "a method of diagnosing kidney cancer comprising: comparing a level of nucleic acid comprising a nucleotide sequence at least 95% identical to SEQ ID NO: 41 in a patient sample…", for example.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which is SEQ ID NO: 41. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

8. Claims 52 and 79-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 52 and 79-94 are broadly drawn to a method for diagnosing kidney cancer, colon cancer, prostate cancer, breast cancer or stomach cancer comprising:

comparing a level of nucleic acid comprising a nucleotide sequence at least 95% identical to SEQ ID NO: 41 in a patient sample comprising human prostate, lung, bladder, breast, stomach or colon tissue to a level of nucleic acid in a control sample, said nucleotide sequence at least 95% identical to SEQ ID NO: 41 encoding a polypeptide with signaling activity; wherein an increase of at least 50% from the level of nucleic acid in the patient sample compared to the level of the nucleic acid in the control indicates that the patient has kidney cancer, colon cancer, prostate cancer, breast cancer or stomach cancer.

However, as will be further discussed, there is no support in the specification for the claimed method. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Working Examples

The specification has no working examples of diagnosing any cancer using a level of expression of SEQ ID NO: 41 or sequences with 95% or 98% sequence identities to SEQ ID NO: 41.

Guidance in the Specification.

The specification provides no evidence that the disclosed nucleic acid sequence with SEQ ID NO: 41 would have usefulness in diagnosing cancer. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses that the polynucleotide with SEQ ID NO: 41 was upregulated in one of twelve renal cell carcinomas (see page 87, Table 14). Therefore, there is no evidence that SEQ ID NO: 41 has diagnostic value even for kidney carcinomas, and certainly no diagnostic value for any other type of cancer. Further, Applicants claim that SEQ ID NO: 41 encodes a polypeptide with signaling activity. No evidence of such activity was provided at the time of invention.

The unpredictability of the art and the state of the prior art

The specification shows that SEQ ID NO: 41 was upregulated in one of twelve renal cell carcinomas (page 87, Table 14). The specification does not provide information on how it was determined that the gene was upregulated. In case it was done by microarray hybridization, the results may not be reliable, as evidenced by the references discussed here. Li et al. (J. Theor. Biol., vol. 219, pp. 539-551, 2002) disclosed that selection of overexpressed genes by either "fold change" or t-test is not reliable method, as the selection of threshold is arbitrary (page 539, last paragraph; page 540, paragraphs one and two). Wang et al. (Bioinformatics, vol. 20, pp. 100-104, 2004) again stresses that either the fold method or t-test method for picking differentially expressed genes are not reliable, since the fold method does not take variations within treatments into consideration, and

the optimal performance of the t-test depends on sample size and assumption that expression intensities have normal distribution (page 100, third and fourth paragraphs). Finally, as pointed out by Dumur et al. (Clin. Chem., vol. 50, pp. 1994-2002, 2004), the quality of RNA or cDNA used in the microarray hybridization affects the outcome of the experiments (page 1995, second paragraph).

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to be able to find out whether SEQ ID NO: 41 or sequences related to it have diagnostic value in any type of cancer, including determining expression levels of SEQ ID NO: 41 or sequences related to it in every possible cancer type and tissue. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the determination of gene upregulation depends on the multitude of factors and the method used, the factor of unpredictability weighs heavily in favor of undue experimentation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

9. No references were found teaching or suggesting claims 52 and 79-94, but they are rejected for reasons given above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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February 1, 2010